PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER		see Form PCT/ISA/220			
P03/252-ve/rg	ACTION		rell as, where applicable, item 5 below.			
International application No.	International filing date (day/mont	h/year)	(Earliest) Priority Date (day/month/year)			
PCT/EP2004/014916	17/11/2004		27/11/2003			
Applicant						
MERCK PATENT GMBH						
This international Search Report has been according to Article 18. A copy is being tra	n prepared by this International Sea	rching Aut	hority and is transmitted to the applicant			
l	This International Search Report consists of a total of					
Basis of the report a. With regard to the language, the language in which it was filed, unline to the language.	international search was carried ou ess otherwise indicated under this l	t on the ba	sis of the international application in the			
The international this Authority (Ru		of a transl	lation of the international application furnished to			
b. With regard to any nucle	otide and/or amino acid sequence	disclosed	I in the International application, see Box No. I.			
2. X Certain claims were fou	nd unsearchable (See Box II).					
3. Unity of invention is lac	king (see Box III).					
4. With regard to the title ,						
X the text is approved as su	ibmitted by the applicant.					
the text has been establis	thed by this Authority to read as followed	ows:				
			•			
5. With regard to the abstract,						
i —	ibmitted by the applicant.					
the text has been establis	shed, according to Rule 38.2(b), by	this Author	ity as it appears in Box No. IV. The applicant rch report, submit comments to this Authority.			
may, within one month it	on the extension making of the interne	36ai	report commonto to and requestry.			
6. With regard to the drawings,						
a. the figure of the drawings to be p		No				
as suggested by	the applicant. is Authority, because the applicant (alled to ev	coest a figure			
	is Authority, because the applicant i is Authority, because this figure bet					
	e published with the abstract.					

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IPC 7	CO7C211/55 CO7C205/57 CO7C255/5 CO7C225/10 A61K31/196 A61K31/13 A61P3/10 A61P9/10		07C317/34 61K31/166				
According to	International Patent Classification (IPC) or to both national classificat	ion and IPC					
B. FIELDS							
IPC 7	Minimum documentation searched (classification system followed by classification symbols) IPC 7 C07C						
		The state of the s	islde soorshod				
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched							
	ata base consulted during the international search (name of data base		ns used)				
EPO-In	ternal, CHEM ABS Data, PAJ, BEILSTEI	N Data, WPI Data					
C. DOCUME	ENTS CONSIDERED TO BE RELEVANT						
Category °	Citation of document, with indication, where appropriate, of the rele	vant passages	Relevant to claim No.				
X	DATABASE CHEMABS 'Online! CHEMICAL ABSTRACTS SERVICE, COLUM OHIO, US; KIZBER, A. I. ET AL: "Transformat the series of diazoamino compound Thermal decomposition of carboxy-substituted diazoaminoben XP002296498 retrieved from STN Database accession no. 1958:34914 abstract & ZHURNAL OBSHCHEI KHIMII , 27, CODEN: ZOKHA4; ISSN: 0044-460X, 1	ions in s. I. zenes" 2208-13	1-4				
X Furt	ther documents are listed in the continuation of box C.	Patent family members are	e listed in annex.				
° Special ca	ategories of cited documents:	'T' later document published after	the international filing date				
A docum	ent defining the general state of the art which is not	or priority date and not in conf cited to understand the princip	flict with the application but				
'E' earlier	dered to be of particular relevance document but published on or after the international	invention "X" document of particular relevant	ce; the claimed invention				
1 docum	filing date cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone						
citatio	which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or comment is combined with one or more other such document.						
other	means nent published prior to the international filing date but than the priority date claimed	ments, such combination beir in the art. *&* document member of the same	ng obvious to a person skilled e patent family				
	e actual completion of the international search	Date of mailing of the internation					
1	17 May 2005	22/06/2005					
Name and	mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2	Authorized officer					
	NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Bedel, C					

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ation) DOCUMENTS CONSIDERED TO BE RELEVANT	Polyvant to claim No.
Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
KNOCHEL PAUL: "A New General Preparation of Polyfunctional Diarylamines by the Addition of Functionalized Arylmagnesium Compounds to Nitroarenes" J.AM.CHEM.SOC., no. 124, 2002, pages 9390-9391, XP002296494 page 9391; example 1d; table 1	1-5
PATENT ABSTRACTS OF JAPAN vol. 0070, no. 19 (C-147), 25 January 1983 (1983-01-25) & JP 57 175106 A (YOSHIO KATSUTA), 28 October 1982 (1982-10-28) voir aussi dans le brevet p.43 dans le tableau les exemples 3,4,8 et 11, les substituants R et Y. abstract	1-5
US 4 316 044 A (ISHIMITSU KEIICHI ET AL) 16 February 1982 (1982-02-16) examples	1-4
GB 1 307 284 A (BOOTS PURE DRUG CO LTD) 14 February 1973 (1973-02-14) page 4, line 4 - page 5, line 2; claim 1 page 8, line 10 - line 18 page 9, line 10 - line 34	1-4,6-8
PATENT ABSTRACTS OF JAPAN vol. 0165, no. 66 (C-1009), 8 December 1992 (1992-12-08) & JP 04 220442 A (SUMITOMO CHEM CO LTD), 11 August 1992 (1992-08-11) see also examples abstract	1-3
US 5 196 610 A (CARR ROBIN A E ET AL) 23 March 1993 (1993-03-23) column 44, line 39 - column 45, line 28; example 36	1-4
WO 03/087045 A (LITTLE PAUL BRIAN; RECEVEUR JEAN-MARIE (DK); ULVEN TROND (DK); 7TM PH) 23 October 2003 (2003-10-23) voir les réactifs utilisés page 79; examples 90-92	1-4
WO 03/076406 A (MERCK PATENT GMBH) 18 September 2003 (2003-09-18) page 26, line 1 - line 23 page 29, line 5 - page 30, line 2; table C	6-14
	KNOCHEL PAUL: "A New General Preparation of Polyfunctional Diarylamines by the Addition of Functionalized Arylmagnesium Compounds to Nitroarenes" J.M.CHEM.SOC., no. 124, 2002, pages 9390-9391, XP002296494 page 9391; example 1d; table 1 PATENT ABSTRACTS OF JAPAN vol. 0070, no. 19 (C-147), 25 January 1983 (1983-01-25) & JP 57 175106 A (YOSHIO KATSUTA), 28 October 1982 (1982-10-28) voir aussi dans le brevet p.43 dans le tableau les exemples 3,4,8 et 11, les substituants R et Y. abstract US 4 316 044 A (ISHIMITSU KEIICHI ET AL) 16 February 1982 (1982-02-16) examples GB 1 307 284 A (BOOTS PURE DRUG CO LTD) 14 February 1973 (1973-02-14) page 4, line 4 - page 5, line 2; claim 1 page 8, line 10 - line 18 page 9, line 10 - line 34 PATENT ABSTRACTS OF JAPAN vol. 0165, no. 66 (C-1009), 8 December 1992 (1992-12-08) & JP 04 220442 A (SUMITOMO CHEM CO LTD), 11 August 1992 (1992-08-11) see also examples abstract US 5 196 610 A (CARR ROBIN A E ET AL) 23 March 1993 (1993-03-23) column 44, line 39 - column 45, line 28; example 36 WO 03/087045 A (LITTLE PAUL BRIAN; RECEVEUR JEAN-MARIE (DK); ULVEN TROND (DK); 7TM PH) 23 October 2003 (2003-10-23) voir les réactifs utilisés page 79; examples 90-92 WO 03/076406 A (MERCK PATENT GMBH) 18 September 2003 (2003-09-18) page 26, line 1 - line 23

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Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	PETER J. O'BRIEN: "A comparison of hepatocyte cytotoxic mechanisms for Cu2+ and Cd2+" TOXYCOLOGY, no. 143, 2000, pages 263-273, XP002296495 table 1 page 269, left-hand column, paragraph 2	6-14
A	GÖNÜL SAHIN: "Effects of some probable antioxidants on the selenite-induced cataract formation and oxidative stres-related paramaters in rats" TOXYCOLOGY, no. 139, 1999, pages 219-232, XP002296496 page 220, left-hand column, paragraph 2 page 223; tables 1,2	6-14
Α .	JEFFERY W. KELLY: "Synthesis, Structure and Activity of Diclofenac Analogues as Transthyretin Amyloid Fibril Formation Inhibitors" J.MED.CHEM., no. 45, 2002, pages 321-332, XP002296497 page 325; table 2	6-14
X	DATABASE BEILSTEIN BEILSTEIN INSTITUTE FOR ORGANIC CHEMISTRY, FRANKFURT-MAIN, DE; XP002328213 Database accession no. 5061244 abstract & GORVIN, JOHN H.: J.CHEM.SOC.PERKIN TRANS.1, 1988, pages 1331-1336,	5
Α	DATABASE BEILSTEIN BEILSTEIN INSTITUTE FOR ORGANIC CHEMISTRY, FRANKFURT-MAIN, DE; XP002328214 Database accession no. 2813438 abstract & LANTZ: BULL.SOC.CHIM.FR., 1956, pages 311-315,	5
X	DATABASE CA CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; WARD YANCEY D.: "Solid phase synthesis of aryl amines via palladium catalysed amination of resin-bound aromatic bromides" XP002328215 Database accession no. 1996:605697 abstract & TETRAHEDRON LETTERS, vol. 37, no. 39, 1996, pages 6993-6996,	5
	vol. 37, no. 39, 1996, pages 6993-6996, 	

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PCT/EP2004/014916

ategory °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE CA CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; BURGER ALFRED: "Some derivatives of 4'-hydroxydiphenylamine-4-carboxylic acid" XP002328216 Database accession no. 1956:44350 abstract & J.A.C.S., no. 77, 1955, page 5733,	5
1	MAFFEI FACINO R ET AL: "ANTIOXIDANT PROFILE OF NIMESULIDE, INDOMETHACIN AND DICLOFENAC IN PHOSPHATIDYLCHOLINE LIPOSOMES (PCL) AS MEMBRANE MODEL" INTERNATIONAL JOURNAL OF TISSUE REACTIONS, BIOSCIENCE EDIPRINT, GENEVA, CH, vol. 15, no. 6, 1993, pages 225-234, XP002048767 ISSN: 0250-0868 the whole document	6-14

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.2

Claims Nos.: 1-4, 6 (partially)

The initial phase of the search revealed a very large number of documents relevant to the issue of novelty. So many documents were retrieved that it is impossible to determine which parts of the claim(s) may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT). For these reasons, a meaningful search over the whole breadth of the claim(s) is impossible. Consequently, the search has been restricted to:
A combination of claims 3-4 as well as claim 5 and a combination of claims 7-9 as well as claim 10.

The use of these compounds as antioxydants has been searched on the full scope of formula (II) (cl.11-14)

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

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Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)		
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:		
1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:		
2. X Claims Nos.: 1-4, 6 (partially) because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:		
see FURTHER INFORMATION sheet PCT/ISA/210		
3. Claims Nos.:		
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).		
Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)		
This International Searching Authority found multiple inventions in this international application, as follows:		
As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.		
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.		
3. As only some of the required additional search fees were timely paid by the applicant, this international Search Report covers only those claims for which fees were paid, specifically claims Nos.:		
4. No required additional search fees were timely paid by the applicant. Consequently, this international Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:		
Remark on Protest The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees.		